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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
08/933,821	09/19/97	GODOWSKI	P P1130

EXAMINER

18N2/1224

KAUFMAN, C

ART UNIT	PAPER NUMBER
1812	3

GENENTECH INC
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SOUTH SAN FRANCISCO CA 94080

DATE MAILED: 12/24/97

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 9/19/97.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 1 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-22 is/are pending in the application.
Of the above, claim(s) _____ is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☐ Claim(s) _____ is/are rejected.
☐ Claim(s) _____ is/are objected to.
☒ Claim(s) 1-22 are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of Reference Cited, PTO-892
☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

DETAILED ACTION

Election/Restriction

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-8, drawn to a NL-1 encoding nucleic acid, host cell, and vector, classified in class 435, subclass 69.1.

II. Claims 1-7, drawn to a NL-5 encoding nucleic acid, host cell, and vector, classified in class 435, subclass 69.1.

III. Claims 1-7, drawn to a NL-8 encoding nucleic acid, host cell, and vector, classified in class 435, subclass 69.1.

IV. Claims 8 and 13-15, drawn to a NL-1 polypeptide and conjugate, classified in class 530, subclass 350.

V. Claims 8 and 13-15, drawn to a NL-5 polypeptide and conjugate, classified in class 530, subclass 350.

VI. Claims 8 and 13-15, drawn to a NL-8 polypeptide and conjugate, classified in class 530, subclass 350.

VII. Claims 9-12 and 13-15, drawn to an antibody and antibody conjugate which specifically binds a NL-1 polypeptide, classified in class 530, subclass 388.24.

VIII. Claims 9-12 and 13-15, drawn to an antibody and antibody conjugate which specifically binds a NL-5 polypeptide, classified in class 530, subclass 388.24.

IX. Claims 9-12 and 13-15, drawn to an antibody and antibody conjugate which specifically binds a NL-8 polypeptide, classified in class 530, subclass 388.24.

X. Claims 16 and 17, drawn to a method of identifying cells expressing a TIE receptor and method of identifying an antagonist of a TIE receptor comprising contacting a cell expressing a TIE receptor with a NL-1 polypeptide, classified in class 435, subclass 7.2.

XI. Claims 16 and 17, drawn to a method of identifying cells expressing a TIE receptor and method of identifying an antagonist of a TIE receptor comprising contacting a cell expressing a TIE receptor with a NL-5 polypeptide, classified in class 435, subclass 7.2.

XII. Claims 16 and 17, drawn to a method of identifying cells expressing a TIE receptor and method of identifying an antagonist of a TIE receptor comprising contacting a cell expressing a TIE receptor with a NL-8 polypeptide, classified in class 435, subclass 7.2.

XIII. Claim 18, drawn to method of imaging by administering an antibody agonist which specifically binds NL-1, class 424, subclass 178.1.

XIV. Claim 18, drawn to method of imaging by administering an antibody agonist which specifically binds NL-5, class 424, subclass 178.1.

XV. Claim 18, drawn to method of imaging by administering an antibody agonist which specifically binds NL-8, class 424, subclass 178.1.

XVI. Claim 18, 19, 21, and 22, drawn to method of imaging and a method of inhibiting vasculogenesis or tumor growth and a method of promoting bone development by administering NL-1, class 514, subclass 12.

XVII. Claim 18, 19, 21, and 22, drawn to method of imaging and a method of inhibiting vasculogenesis or tumor growth and a method of promoting bone development by administering NL-5, class 514, subclass 12.

XVIII. Claim 18-22, drawn to method of imaging and a method of inhibiting vasculogenesis or tumor growth and a method of promoting bone development by administering NL-8, class 514, subclass 12.

2. The inventions are distinct, each from the other because of the following reasons:

First, it is important to set forth that ligands NL-1, NL-5, and NL-8 are distinct for several reasons. The nucleic acid encoding each ligand has a distinct pattern and level of tissue expression. The nucleic acid encoding NL-8 has an expression pattern distinct from that of NL-1 or NL-5 (p. 55, line 7-8 of specification). Also the level of expression of NL-1 and NL-5 was different (p. 54, lines 12-14), as was the pattern of expression, *e.g.,* NL-1 is expressed in cartilage, while NL-5 is expressed in placenta (p.54, line 13. through p. 55, line 4). While the polypeptides share as a common structure a fibrinogen domain, the domains of NL-1, NL-5, and NL-8 are only 64-74% identical (p. 53, lines 20-24). Likewise, the sequence of other regions of the ligands are different. Additionally, while these three ligands bind a TIE receptor, there is no indication that all three bind the same receptor. So because these ligands are structurally distinct, have different encoding nucleic acid expression patterns and levels, and because they are not disclosed as having the same receptor specificity, each ligand and nucleic acid encoding each ligand constitutes an independent and distinct invention. Because the ligands are distinct, an antibody specific to one ligand is distinct from an antibody specific for another ligand. The antibodies would be expected to be structurally different in their variables regions and one specific antibody would not reasonably be expected to bind all ligands, especially in view of the sequence differences of the ligands. These reasons form the basis of separating inventions relating to each of the ligands, that is, the basis for distinctness of inventions 1-III, IV-VI, VII-IX, X-XII, or XIII-XVIII.

Inventions I-III and IV-VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together, or they have different modes of operation, or they have different functions, or they have different effects. (MPEP § 806.04, MPEP § 808.01). In the instant case the nucleic acids are distinct from the polypeptides because they are structurally distinct and have different functions--encoding a polypeptide versus interacting with other polypeptides, respectively.

Inventions I-III and VII-IX are unrelated. The nucleic acid and antibody are structurally distinct, cannot be used together and have different functions--encoding a polypeptide versus binding a polypeptide.

Inventions I-III are unrelated to the methods of inventions X-XII, XIII-XV, and XVI-XVIII. In the instant case the different inventions cannot be used together because none of the methods of inventions X-XII, XIII-XV, or XVI-XVIII can be used with a nucleic acid, but instead require an antibody or ligand. Also, the methods cannot be used to produce a nucleic acid.

Inventions IV-VI and VII-IX are unrelated. The ligand is structurally different from the antibody of inventions VII-IX. Also, the ligand and antibody have different functions--one binds a receptor and the other binds the ligand. While the ligand can be used to make the antibody, it can also be used for other purposes, such as affinity purification of its cognate receptor.

Inventions IV-VI are related to inventions X-XII and XVI-XIII as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the ligand can be used in a materially different process such as in the production of a cognate antibody.

Inventions IV-VI and XIII-XV are unrelated. The ligands of Inventions IV-VI cannot be made by or used in the method of Inventions XIII-XV because that method requires the use an antibody.

Inventions VII-IX are unrelated to the methods of inventions X-XII and XVI-XVIII. The antibodies of Inventions VII-IX cannot be used in or made by the methods, which require the use of a ligand to the receptor, not an antibody which specifically binds the ligand.

Inventions VII-IX are related to inventions XIII-XV as product and process of use. However, the antibodies of inventions VII-IX can be used in a materially different process such as in the affinity purification of the ligands they specifically bind to.

The method of inventions X-XII is unrelated to the methods of inventions XIII-XV and XVI-XIII. These methods have different effects--identifying cells expressing a TIE receptor versus a diagnostic method and/or method of treatment. Also, these methods have different modes of operation--monitoring ligand binding versus monitoring angiogenesis or administration of an effective amount of ligand.

The method of inventions XIII-XV is unrelated to the method of inventions XVI-XIII. These methods have different modes of operation because inventions XIII-XV require an antibody which specifically binds to a cognate ligand, but inventions XVI-XIII require a ligand which binds to a TIE receptor.

Because these inventions are distinct for the reasons given above, have acquired a separate status in the art as shown by their different classification and because of their recognized divergent subject matter (*e.g.*, structurally and functionally distinct polypeptides or nucleic acids, methods with different effects or modes of operation), and the search required for each invention is not coextensive with the other, restriction for examination purposes as indicated is proper.

3. A telephone call was made to Ginger R. Dreger on 12/16/97 to request an oral election to the above restriction requirement, but did not result in an election being made.

Applicant is advised that the response to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

4. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any

amendment of inventorship must be accompanied by a diligently-filed petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(h).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Claire M. Kaufman, whose telephone number is (703) 305-5791. Dr. Kaufman can generally be reached Monday through Friday from 8:00AM to 4:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Stephen Walsh, can be reached at (703) 308-2957.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. NOTE: If applicant *does* submit a paper by fax, the original signed copy should be retained by the applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office. **Please** advise the examiner at the telephone number above before facsimile transmission.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [**stephen.walsh@uspto.gov**].

All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

cmk
December 23, 1997

Stephen Walsh
STEPHEN WALSH
SUPERVISORY PATENT EXAMINER
GROUP 1800